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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,169	06/08/2001	Clemens Antoni Van Blitterswijk	04148-00012	9604

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07/29/2003

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EXAMINER

DEBERRY, REGINA M

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 07/29/2003

(/)

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/877,169

Applicant(s)

VAN BLITTERSWIJK ET AL.

Examiner

Regina M. DeBerry

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-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10 and 13-28 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10, 13-20, 22, 23, 25, 26 and 28 is/are rejected.
- 7) ☒ Claim(s) 21, 24 and 27 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/621178, 08/810266.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 20 May 2003 (Paper No. 9) has been entered.

The amendment filed 20 May 2003 (Paper No. 10) has been entered in full. Applicant's election with traverse of Group in Paper No. is acknowledged. Claims 10, 13-28 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejections of claims 20-28 under 35 U.S.C. 102(b) as being anticipated by Gronthos *et al.* (IDS, submitted by Applicant, Paper No. 5; Blood, Vol. 84/12 4164-4173, 1994) as set forth at pages 4-5 of the previous Office Action (27 February 2003, Paper No. 7) is *withdrawn* in view of Applicant's convincing argument regarding osteocalcin inhibiting bone formation (20 May 2003, Paper No. 10).

Claim Rejections - 35 USC § 112

Claims 10, 13-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. The basis for this rejection is set forth at pages 3-4 of the previous Office Action (27 February 2003, Paper No. 7).

Applicant maintains that the specification provides adequate support for the limitations of claim 10 and claims depending therefrom. Applicant directs the Examiner's attention to Example 3, page 6, line 32; page 8, lines 4-6; page 7, lines 6-12 and page 5, lines 2-6, 14-16 and 23-24.

Applicant's arguments have been fully considered but not deemed persuasive. The pages Applicant has pointed out do not teach those steps as recited in claim 10: a method of producing active factors comprising the steps of applying undifferentiated mammalian cells on a substrate, contacting the cells with a culture medium for a sufficient time to produce a matrix, contacting the cells with the culture medium for a sufficient time to produce active factors, removing the substrate and the matrix from the culture medium; and recovering the active factors from the culture medium. Furthermore, claim 10 is drawn to applying undifferentiated mammalian cells on a substrate. Page 8, lines 4-6; as recited by Applicant, employs the use of osteoblast which are differentiated (page 1, lines 29) not undifferentiated cells. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10, 13-16, 18, 20, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Gazit *et al.*, Connective Tissue Research, Vol. 23, pages 153-161, 1989.

The instant claims are drawn to a method of producing active factors comprising the steps of: (a) applying undifferentiated cells on a substrate (b) contacting the cells with a culture medium for a sufficient time to produce a matrix; (c) contacting the cells with the culture medium for a sufficient time to produce active factors; (d) removing the substrate and matrix from the culture medium; and (e) recovering the active factors from the culture medium.

The instant claims are also drawn to a method of producing bone growth factors comprising the steps of (a) applying bone marrow cells on a substrate; (b) contacting the bone marrow cells with a culture medium for a sufficient time to produce bone growth factors; and (c) removing the substrate and the cells from the cultured medium; and (d) recovering the bone growth factors from the culture medium.

Gazit *et al.* teach the preparation of healing marrow condition medium (HBMC). Gazit *et al.* teach that the tissue was separated from the marrow space of rat tibiae and incubated for 24 hours in serum-free F-10 medium supplemented with penicillin-streptomycin (**claims 15, 16, 18, 22**). The medium was then collected and boiled for 10

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minutes (**claim 10**)(page 154, 3rd paragraph). Gazit *et al.* teach that the growth factor activity (GFA) from the HBMC was monitored by examining the effects on DNA synthesis in a culture of osteogenic ROS 17/2 cells (**claims 13, 14 and 23**)(page 154, 4th paragraph; page 155, 6th paragraph and page 156, Figure 1).

Claims 25, 26 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Gleave *et al.*, The Journal of Urology, Vol. 147, 1151-1159, 1992.

The instant claims are drawn to a method of producing growth factors comprising the steps of: (a) applying stromal cells on a substrate; (b) contacting the stromal cells with a culture medium for a sufficient time to produce growth factors; (c) removing the substrate and the cells from the culture medium; and (d) recovering the growth factors from the culture medium.

Gleave *et al.* teach that conditioned media from bone and prostate fibroblasts (stromal) stimulated LNCaP cell growth both *in vitro* and *in vivo*. Gleave *et al.* state that the results demonstrate that both endocrine and paracrine factors are important in prostate cancer growth, and that stromal microenvironments influence disseminated tumor cell growth (page 1152, lines 4-9). Gleave *et al.* teach how to determine the mitogenic effect of fibroblast conditioned media on LNCaP growth *in vivo* and *in vitro*. Conditioned media was collected from fibroblast cells (**claims 25, 26**)(page 1152, 2nd-3rd paragraph and page 1153, 1st paragraph). Gleave *et al.* examine the growth factor production by stromal cells. Gleave *et al.* teach that bFGF is variably expressed in all

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fibroblasts cell lines, but most strongly by MS bone and NbF-1 prostate fibroblast (page 1155, 2nd paragraph and Figure 5b). Gleave *et al.* compare the mitogenic activity of conditioned media from different fibroblast cell lines on LNCaP growth *in vitro* and *in vivo* (**claim 28**)(page 1156 and Figures 7 and 8).

Conclusion

Claims 21, 24 and 27 are objected to.

Claims 10, 13-20, 22, 23, 25, 26 and 28 are rejected.

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on 9:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



RMD
July 25, 2003



GARY KUNZ
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